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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/610,034	07/05/2000	Xin-Xing Gu	NIH142.001C1	4610

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EXAMINER

SHAHNAN SHAH, KHATOL S

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 12/02/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/610,034

Applicant(s)

GU ET AL.

Examiner

Khatol S Shahnan-Shah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 39-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 39-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on August 30, 2002 has been entered.
2. Claims 1-4 and 6-34 have been canceled without prejudice. Claims 39-47 are pending and under consideration.

### ***Drawings***

3. The formal drawings submitted August 30, 2002 are approved by the Draftsperson.

### ***Prior Citations of Title 35 Sections***

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

### ***Prior Citations of References***

5. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No forms PTO-892 and PTO-1449 have been submitted with this office action.

### ***Rejection Moot***

6. Rejection of claims 1-4 and 6-34 under 35 USC 103 made in paragraph 10 of the office action mailed March 26, 2002 is moot in view of applicants' cancellation of the claims.

***Rejection Withdrawn***

7. Rejection of claims 39-47 under 35 USC 103 made in paragraph 10 of the office action mailed March 26, 2002 is withdrawn in view of applicants' amendments.

***New Rejection***

8. Claims 39-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gu et al. (U.S. Patent Number 6,207,157) in view of Vaneeschoutte et al. (Journal of Clinical Microbiology, Vol. 28, No.2, pp. 182-187, 1990.), Campagnari et al. (Microbial Pathogenesis, Vol. 8, pp. 353-362, 1990) and Edebrink et al. (Carbohydrate research Vol. 257, pp.269-284, 1994).

Note: Prior to establishing a prima facie case of obviousness the examiner wants to emphasize on the similarities and structure of lipooligosaccharides (LOS) and detoxified LOS (dLOS) in gram-negative bacteria and their role in production of immunogenic composition.

Major studies have been done on the LOS of *Neisseria meningitidis* (Gu et al., Infection and Immunity, Vol. 61, No. 5, pp. 1873-1880, May 1993), *Haemophilus influenzae* (Gu et al., Infection and Immunity, Vol. 63, No. 10, pp. 4115-4120, Oct, 1995; Gu et al., Infection and Immunity, Vol. 64, No. 10, pp. 4047-4053, Oct 1996; and Gu et al., Infection and immunity, Vol. 65, No. 11, pp. 4488-4493, Nov. 1997), *Vibrio cholera* (Gupta et al. Infection and Immunity, Vol. 60, No. 8, pp. 3201-3208, August, 1992) as potential vaccines. Also it is well known in the art that genera *Moraxella* (*Branhamella*), *Hemophilus* and *Neisseria* contain important human pathogens that can share ecological niches on mucosal surfaces. These non-enteric bacteria have outer membranes typical of gram-negative bacteria but their lipooligosaccharides lack O-antigenic side chain (Campagnari et al. Microbial Pathogenesis, Vol. 8, pp. 353-362, 1990). Campagnari et al. further teach that studies indicate that conservation of

LOS exists among these organisms (see abstract and page 360). Edebrink et al. (Carbohydrate research Vol. 257, pp.269-284, 1994) teach structure of lipooligosaccharide isolated from *Moraxella catarrhalis*. Edebrink et al. teach that the lipopolysaccharide of *Moraxella catarrhalis* lacks O-antigenic side chains characteristic of enteric bacteria, thus being similar in general structure to the lipopolysaccharides of *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae* and *Bordetella pertussis* (see page 270).

The instant claims are drawn to an immunogenic composition comprising lipooligosaccharide isolated from *Moraxella catarrhalis* and detoxified by treating to remove esterified fatty acids to produce detoxified LOS (dLOS) and an immunogenic carrier covalently linked thereto.

Gu et al. teach an immunogenic composition comprising an isolated lipooligosaccharide detoxified by treating to remove esterified fatty acids to produce detoxified LOS (dLOS) and an immunogenic carrier covalently linked thereto (see abstract).

Gu et al. teach a conjugate vaccine for *Haemophilus influenzae* comprising lipooligosaccharide (LOS) from which esterified fatty acids have been removed conjugated to an immunogenic carrier. The vaccine is useful for prevention of otitis media and respiratory infections in mammals (see abstract). They also teach a LOS from which esterified fatty acids have been removed from lipid A to form a detoxified LOS (dLOS), and an immunogenic carrier (a protein) covalently linked thereto (see claims 1 and 2). They further teach, wherein immunogenic carrier protein is selected from the group consisting of tetanus toxin/toxoid, a high molecular weight (HMP) isolated from nontypeable *Haemophilus influenzae*, diphtheria toxin/toxoid, detoxified *P. aeruginosa* toxin A, cholera toxin/toxoid, pertussis toxin/toxoid and more (see claim 3). They too

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teach alum as an adjuvant (see claims 10-11). They also teach linker compounds such as adipic acid dihydrazide,  $\epsilon$ -aminohexanoic acid, chlorohexanol dimethyl acetal, D- glucuronolactone and p-nitrophenylethyl amine (see claims 5-7). Gu et al. do not teach *Moraxella catarrhalis*. However, Vaneechoutte et al. teach immunogenic compositions comprising lipooligosaccharide isolated from *Moraxella (Barnhamella) catarrhalis* (see abstract and material and method page 182).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to detoxify the isolated lipooligosaccharides of Vaneechoutte et al. in view of teachings by Gu et al. to obtain the instant disclosure. Given the art-recognized fact that lipooligosaccharide epitopes shared among gram-negative non-enteric mucosal pathogens such as *Haemophilus influenzae* and *Moraxella catarrhalis* (Campagnari et al., see abstract, title and introduction) and the teaching of Edebrink et al. that the lipopolysaccharide of *Moraxella catarrhalis* lacks O-antigenic side chains characteristic of enteric bacteria, thus being similar in general structure to the lipopolysaccharides of, *Haemophilus influenzae* (see page 270) it would have been obvious to one having ordinary skill in the art to detoxify *Moraxella catarrhalis* lipopolysaccharide in view of teachings by Gu et al.

One having ordinary skill in the art would have been motivated by expectation of success and the attainment of a better composition and the fact that Gu et al. teach unexpected result that the dLOS conjugates obtained following detoxification are dramatically more effective than LOS (see figure 1) to modify the isolated lipooligosaccharides from *Moraxella catarrhalis* to make an immunogenic composition.

*Conclusion*

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

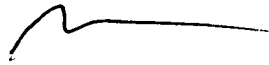
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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November 20, 2002



MARK NAVARRO  
PRIMARY EXAMINER